NORTHRUP EXHIBIT H

5/11/92

BSAC

Key features:

PCR or thermal-cycle driven enzymatic reactions, but includes other DNA (or other biochem or chem) reactions

All techns. involving reaction-based methodologies

Ability to integ elec, mechn or optical comps. using microfab techs:

Reaction parameter control: heating, pumping, circulating, cooling

Reaction or reagent detection - manipulation

WJE: Appl. disclosed Fig. 2 chamber & specific sys. for carrying out PCR reactions. What are minimum comps. of such a system?

in Fig. 1

Biochem reaction manip, control + detection: ① lamb-wave devices - to pp, mix + detect, ② electrokinetic effects to pp, sep or process; ③ integ - T control devices; ④ optical filters; ⑤ chamber w/ heating elements

Detect: mass changes, density + viscosity

(2)

1/11/92

MIT Allen Northrup
Dick White

→ thermal cycling

claim: mixing chamber; also clean system

Micro liter vols → used in system
Smaller — can be done faster
and less power.

96°↔55°C → heat + cool.
system on

Re-packaged/chips → novel:
integ. on chips.

* PCR or any other chem. or bio-chem reaction that requires thermal cycling.

Monolithic, microfab device →
1st time such a sys was been done on this scale

(micropumps) (3)

Use of hand-crank as p.p. → moves particles in single file
* check to see if I have file on white's US 5,006,749.

Unique: microheaters in chamber key part of inv. / system.

Fiber optic inside reaction chamber for detection.

PCR technique now take about ~~1 or 2 hrs~~ 1 to 5 minutes ~~at inv. can get results w/i 1 to 5 minutes.~~ Fantastic impr. in time. ~ can get results w/i a few seconds. re cycles on the order of a cycle. Due to small vol. + high surface area.
could be portable + wash w/ battery. as opposed to 110v.

~~T diff + surface~~
Reactions dep. on concentration
* ...

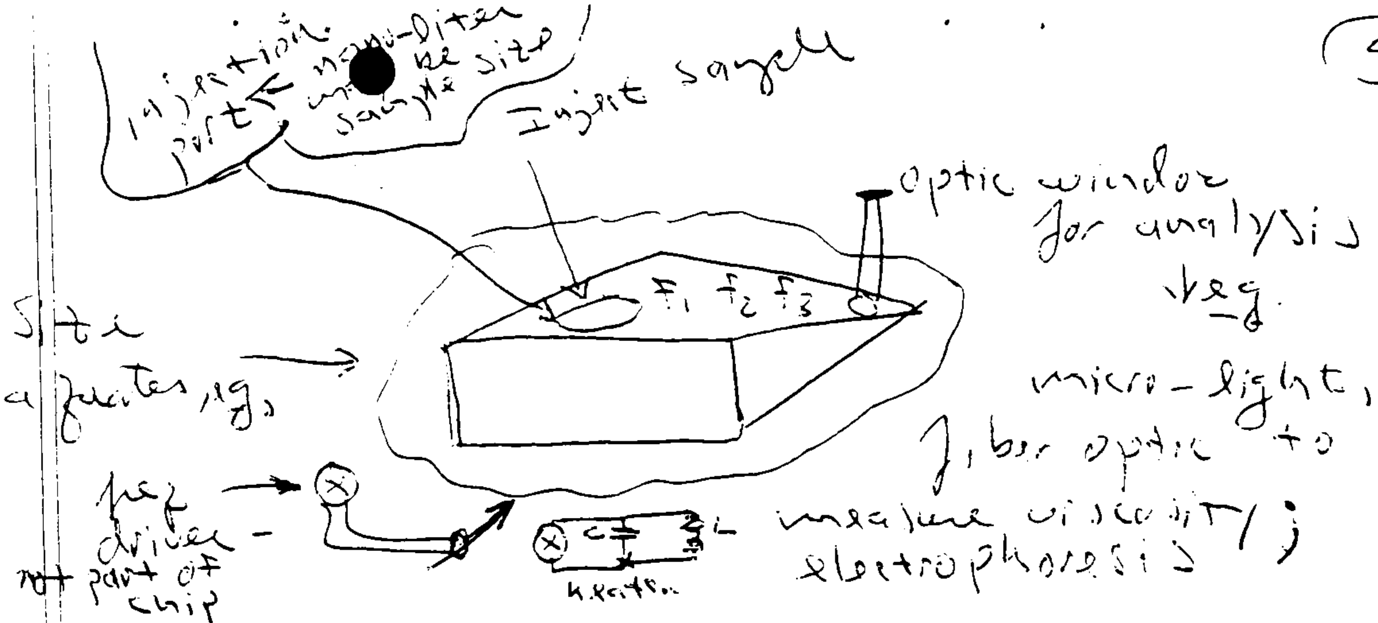
on → 3 volts is 96° C based on heater Res.
off → 1/2 volts is 55° C " "

Monolithic Fab – is very important
– can do in batches on
wafer. Thus they are
cheap & are disposable.

* Need spec. sheet for chamber
fabrication

PPling in chamber – see Dick
White

chamber – includes ultrasonic
agitator for mixing.
↓ Also useful for cell lysing



pump, mixer etc run a diff freq's (F_1, F_2 F_3) so can turn diff comp on & off by operating a diff freqs. Heating is also done by tuning F_4 for heater:

Key doing PCR on chip w/ reaction chamber.

Materials used in chamber can negatively effect PCR reaction eg [illegible] divalent cations will prevent PCR from doing.

Reactants on chip in advance & sold as a unit.

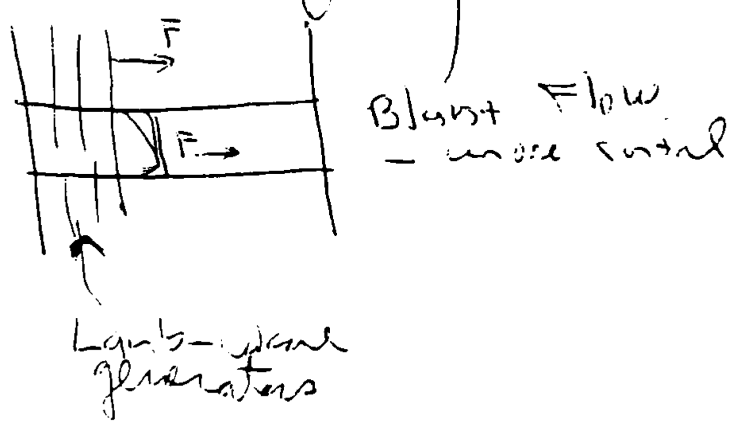
Using surface tension to maintain reactant

Possible talks / pubs: none on the HORZ; Oct 1992

Draft appl to Inventors by / beginning to mid-June + file by end of June

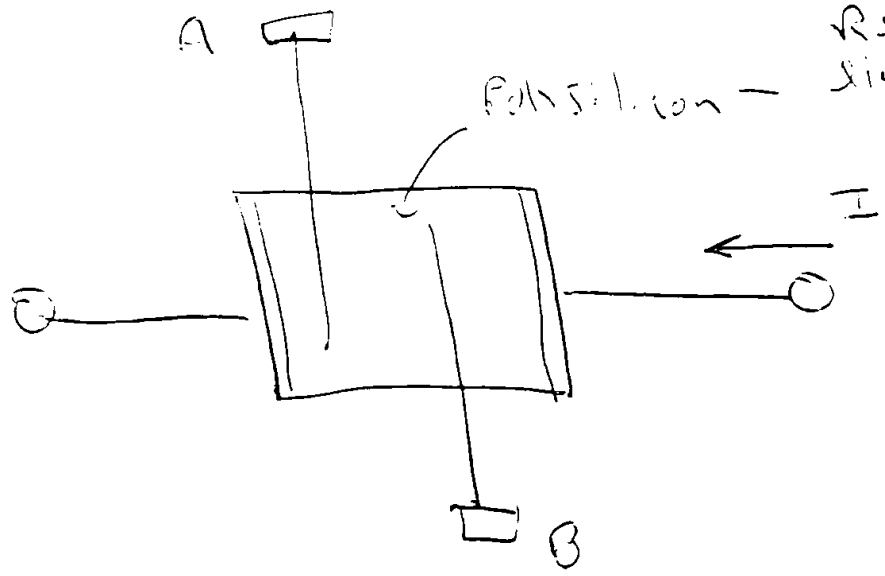
* Remote drive

Advs: All parts of channels moved at same speed - adv. of vari-vane PP.



See White's US 5,006,749

- control → Nice feature:



- Use ~~electrodes~~ electrodes A & B to measure change. Send in known current I & measure voltage bet. electrodes A & B.

- This detail should be in drug.

SiO_2 – is material at bottom of chamber; std material handled by bio-chemists

DNA probes – in chamber; parts attach to probes + sensor detect mass change as known base attachments to probes.